

Unmet needs of high-risk mothers reduce success of antiretroviral treatment in HIV-infected infants

Effective prevention of mother-to-child transmission (PMTCT) programmes have dramatically reduced new paediatric HIV infections, and increasing access to antiretroviral therapy (ART) has substantially improved outcomes in infected children.^[1-3] However, unmet needs persist in paediatric HIV infection.^[4] In an ongoing study of early infant diagnosis and ART initiation following *in utero* transmission in KwaZulu-Natal Province, South Africa, we observe that the same factors predisposing to mother-to-child transmission (MTCT) in the current era of effective prevention are precisely those that militate against the success of ART for infected infants. Four cases are described to illustrate that the unmet needs of the high-risk mother have to be addressed urgently in order to achieve successful treatment of the infected child.

M1 is a 21-year-old mother who herself became HIV-infected as a result of MTCT. M1's mother died from HIV-related conditions when M1 was 10 years of age. Disclosure of M1's HIV status was at 13 years. Thereafter, adherence became problematic as she navigated adolescence without parental support. Now living with her partner's family, she feels unable to disclose her HIV status. At 18 years of age she had her first child, who died at 12 months, HIV status unknown. Two years later, she had a second child who was diagnosed as HIV-infected on the day of birth; ART was initiated at 20 hours of age. Because M1 needed to hide the medication, giving ART to her baby was erratic. The child's viral load (VL) became undetectable at 2 months of age, but rebounded the following month and has remained unstable since then.

M2 is a 17-year-old mother whose first child had been born 2 years previously with intrauterine HIV infection. M2 recently delivered her second baby at 28 weeks' gestation after a pregnancy without antenatal care. This child is also HIV-infected. M2 lives at home with her parents, having left secondary school prematurely. She has suffered from substance abuse and partner violence. M2 and the first HIV-infected child remain virologically unsuppressed, although the first child achieved an undetectable VL at 2 months of age. The VL of the second child is not known.

M3 is a 30-year-old married woman. She and her husband both have secondary education and are both employed. M3 first tested HIV-positive at 28 weeks' gestation and was told that taking ART would prevent the possibility of her transmitting the virus to her child. The baby's initial HIV test was indeterminate and the VL was undetectable. Repeat testing confirmed that the baby was HIV-infected. When told that the baby was infected, M3 said she had lost faith in ART, since she denied missing any doses during pregnancy. Subsequently, M3 has struggled to take her own therapy consistently or to administer ART to the infant, and both mother and child remain virally unsuppressed.

M4 is a 22-year-old mother who was orphaned in early childhood. Because of domestic violence at the hands of her extended family, she lived in a home of safety. She defaulted from ART prior to and during pregnancy owing to non-disclosure issues. She delivered a 1 400 g baby at 29 weeks' gestation. The baby had an extended hospital stay because of multiple medical conditions associated with prematurity.

Table 1. Psychosocioeconomic and clinical factors influencing antiretroviral treatment outcome in four mother-child pairs following *in utero* HIV transmission

Patient features	Case 1	Case 2	Case 3	Case 4
Mother				
Psychosocial/family	<ul style="list-style-type: none"> • Loss of mother in childhood, lack of family support • Dependence on partner and partner's family for accommodation • Non-disclosure to partner/partner's family • First child at age 18 years 	<ul style="list-style-type: none"> • Left school early – lack of education and life skills • Substance abuse • Partner violence • First child at age 15 years • Second child at age 17 years 	<ul style="list-style-type: none"> • Stable, married, well educated; patient and husband employed • The ability of ART adherence to reduce the risk of MTCT was not fully explained 	<ul style="list-style-type: none"> • Orphaned in early childhood, lived in home of safety • Domestic violence in extended family • Non-disclosure to extended family prior to delivery
Clinical	<ul style="list-style-type: none"> • Chronic HIV infection from birth • Declining CD4+ cell count, persistent viraemia 	<ul style="list-style-type: none"> • No antenatal care • Viraemia unsuppressed 	<ul style="list-style-type: none"> • VL 350 copies/mL at delivery; latest VL 9 700 copies/mL 	<ul style="list-style-type: none"> • VL 330 000 copies/mL at delivery; latest VL <20 copies/mL at 1 month
Child				
Psychosocial/family	<ul style="list-style-type: none"> • Sibling died at 12 months of age • Maternal non-disclosure, non-adherence 	<ul style="list-style-type: none"> • Two children with HIV infection • Maternal non-disclosure, non-adherence 	<ul style="list-style-type: none"> • Mother has lost faith in ART • Non-adherence despite disclosure 	<ul style="list-style-type: none"> • Mother reconciled with her family, facilitating disclosure and ART adherence
Clinical	<ul style="list-style-type: none"> • Persistent viraemia 	<ul style="list-style-type: none"> • Younger sibling premature at 28 weeks' gestation • Persistent viraemia 	<ul style="list-style-type: none"> • Initial VL <100 copies/mL; VL 1 600 copies/mL at 2 months 	<ul style="list-style-type: none"> • Premature at 29 weeks' gestation, multiple neonatal complications • VL at birth 3 000 copies/mL; VL <20 copies/mL at 1 month

ART = antiretroviral therapy; MTCT = mother-to-child transmission; VL = viral load.

The prolonged hospital stay provided an opportunity for intervention including social worker involvement, allowing reconciliation between M4 and her partner's family and disclosure of her HIV diagnosis to them. The baby initiated ART within the first 48 hours of life and reached an undetectable VL at 1 month of age. Both mother and baby have remained virologically suppressed to date without viral blips or rebound.

These four case studies illustrate several general features we have observed among the study cohort of *in utero*-infected infants and their mothers as a whole. In many cases the same factors that have destabilised the lives of mothers, and that contribute to HIV transmission, are those that interfere with effective treatment of HIV in the infants. In contrast, in the same setting in KwaZulu-Natal but 15 years ago, in the era prior to effective PMTCT, ART adherence levels of $\geq 95\%$ and virological suppression rates of 100% were seen in infants at 1 year post ART.^[5] At that time, MTCT rates were high^[2] and there was no self-selection for non-adherence in those mothers.

The psychosocioeconomic factors set out in Table 1 play a critical role in determining ART adherence and therefore virological suppression in mother and child. Central among these is non-disclosure of HIV status to household members, as noted in other African studies.^[4,6] The struggle for survival experienced by many of these women takes priority over risking disclosure of HIV status, since in many cases the mother is entirely dependent on her partner for the basic needs of food and housing. Striking a balance between the two fundamental life issues of caring for an HIV-infected child and personal survival requires an open dialogue between healthcare providers and receivers of healthcare.

The fourth case described above illustrates what can be achieved in difficult circumstances. In this instance, the child was premature and initially unwell, requiring many weeks of hospital admission. This provided the opportunity for relationships to be established between social workers and the family, ultimately resulting in a successful outcome. In contrast, what is more typically observed is the lost opportunity to achieve rapid suppression of viraemia in newborns diagnosed in the first days of life. Indeed, in case 3, the infant had undetectable plasma viraemia initially, having received trans-placental ART. However, despite the parents – unusually – being married, educated and employed, the mother had become disillusioned with ART, having been poorly counselled during pregnancy.

In summary, in the era of effective PMTCT, the same psychosocioeconomic factors that predispose to mother-to-child transmission also substantially increase the likelihood of ART failure in infected infants. For this reason, maximal efforts now need to be invested in addressing the fundamental challenges faced by these high-risk mothers, since only then will the benefits of early infant diagnosis be fully realised.

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